

variable domain, and further comprising a Framework Region (FR) amino acid substitution at a site selected from the group consisting of:

4L, 35L, 38L, 43L, 44L, 46L, 58L, 62L, 64L, 65L, 66L, 67L, 68L, 69L, 73L, 85L, 98L, 2H, 4H, 36H, 39H, 43H, 45H, 69H, 70H, 74H, 75H, 76H, 78H, and 92H, utilizing the numbering system set forth in Kabat.

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